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TECH CENTER 1600/2900

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Demo, Susan
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Rigel Pharmaceuticals, Inc.

<120> MRE11: Modulation of Cellular Proliferation

<130> 021044-001310US

<140> US 10/026,331

<141> 2001-12-21

<150> US 60/309,737

<151> 2001-08-01

<160> 21

<170> PatentIn Ver. 2.1

<210> 1

<211> 2537

<212> DNA

<213> Homo sapiens

<220>

<223> human MRE11 meiotic recombination 11 homolog A

<220>

<221> CDS

<222> (171)..(2297)

<223> MRE11

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<213> Homo sapiens

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<400> 2

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Gly Asn Asp Thr Phe Val Thr Leu Asp Glu Ile Leu Arg Leu Ala Gln
          35          40          45
Glu Asn Glu Val Asp Phe Ile Leu Leu Gly Gly Asp Leu Phe His Glu
          50          55          60
Asn Lys Pro Ser Arg Lys Thr Leu His Thr Cys Leu Glu Leu Leu Arg
          65          70          75          80
Lys Tyr Cys Met Gly Asp Arg Pro Val Gln Phe Glu Ile Leu Ser Asp
          85          90          95
Gln Ser Val Asn Phe Gly Phe Ser Lys Phe Pro Trp Val Asn Tyr Gln
          100          105          110
Asp Gly Asn Leu Asn Ile Ser Ile Pro Val Phe Ser Ile His Gly Asn
          115          120          125
His Asp Asp Pro Thr Gly Ala Asp Ala Leu Cys Ala Leu Asp Ile Leu
          130          135          140
Ser Cys Ala Gly Phe Val Asn His Phe Gly Arg Ser Met Ser Val Glu
          145          150          155          160
Lys Ile Asp Ile Ser Pro Val Leu Leu Gln Lys Gly Ser Thr Lys Ile
          165          170          175
Ala Leu Tyr Gly Leu Gly Ser Ile Pro Asp Glu Arg Leu Tyr Arg Met
          180          185          190
Phe Val Asn Lys Lys Val Thr Met Leu Arg Pro Lys Glu Asp Glu Asn
          195          200          205
Ser Trp Phe Asn Leu Phe Val Ile His Gln Asn Arg Ser Lys His Gly
          210          215          220
Ser Thr Asn Phe Ile Pro Glu Gln Phe Leu Asp Asp Phe Ile Asp Leu
          225          230          235          240
Val Ile Trp Gly His Glu His Glu Cys Lys Ile Ala Pro Thr Lys Asn
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Ile	Lys	Gly	Arg	Lys	Met	Asn	Met	His	Lys	Ile	Pro	Leu	His	Thr	Val			
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Arg	Gln	Phe	Phe	Met	Glu	Asp	Ile	Val	Leu	Ala	Asn	His	Pro	Asp	Ile			
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Phe	Asn	Pro	Asp	Asn	Pro	Lys	Val	Thr	Gln	Ala	Ile	Gln	Ser	Phe	Cys			
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Leu	Glu	Lys	Ile	Glu	Glu	Met	Leu	Glu	Asn	Ala	Glu	Arg	Glu	Arg	Leu			
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Gly	Asn	Ser	His	Gln	Pro	Glu	Lys	Pro	Leu	Val	Arg	Leu	Arg	Val	Asp			
			355					360					365					
Tyr	Ser	Gly	Gly	Phe	Glu	Pro	Phe	Ser	Val	Leu	Arg	Phe	Ser	Gln	Lys			
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Phe	Val	Asp	Arg	Val	Ala	Asn	Pro	Lys	Asp	Ile	Ile	His	Phe	Phe	Arg			
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His	Arg	Glu	Gln	Lys	Glu	Lys	Thr	Gly	Glu	Glu	Ile	Asn	Phe	Gly	Lys			
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Leu	Ile	Thr	Lys	Pro	Ser	Glu	Gly	Thr	Thr	Leu	Arg	Val	Glu	Asp	Leu			
			420					425							430			
Val	Lys	Gln	Tyr	Phe	Gln	Thr	Ala	Glu	Lys	Asn	Val	Gln	Leu	Ser	Leu			
			435					440							445			
Leu	Thr	Glu	Arg	Gly	Met	Gly	Glu	Ala	Val	Gln	Glu	Phe	Val	Asp	Lys			
			450				455					460						
Glu	Glu	Lys	Asp	Ala	Ile	Glu	Glu	Leu	Val	Lys	Tyr	Gln	Leu	Glu	Lys			
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Thr	Gln	Arg	Phe	Leu	Lys	Glu	Arg	His	Ile	Asp	Ala	Leu	Glu	Asp	Lys			
						485				490					495			
Ile	Asp	Glu	Glu	Val	Arg	Arg	Phe	Arg	Glu	Thr	Arg	Gln	Lys	Asn	Thr			
			500					505							510			
Asn	Glu	Glu	Asp	Asp	Glu	Val	Arg	Glu	Ala	Met	Thr	Arg	Ala	Arg	Ala			
			515					520					525					
Leu	Arg	Ser	Gln	Ser	Glu	Glu	Ser	Ala	Ser	Ala	Phe	Ser	Ala	Asp	Asp			
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Leu	Met	Ser	Ile	Asp	Leu	Ala	Glu	Gln	Met	Ala	Asn	Asp	Ser	Asp	Asp			
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Ser	Ile	Ser	Ala	Ala	Thr	Asn	Lys	Gly	Arg	Gly	Arg	Gly	Arg	Gly	Arg			
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Arg	Gly	Gly	Arg	Gly	Gln	Asn	Ser	Ala	Ser	Arg	Gly	Gly	Ser	Gln	Arg			
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Gly	Arg	Ala	Asp	Thr	Gly	Leu	Glu	Thr	Ser	Thr	Arg	Ser	Arg	Asn	Ser			
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Lys	Thr	Ala	Val	Ser	Ala	Ser	Arg	Asn	Met	Ser	Ile	Ile	Asp	Ala	Phe			
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Lys	Ser	Thr	Arg	Gln	Gln	Pro	Ser	Arg	Asn	Val	Thr	Thr	Lys	Asn	Tyr			
625						630					635				640			
Ser	Glu	Val	Ile	Glu	Val	Asp	Glu	Ser	Asp	Val	Glu	Glu	Asp	Ile	Phe			
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Pro	Thr	Thr	Ser	Lys	Thr	Asp	Gln	Arg	Trp	Ser	Ser	Thr	Ser	Ser	Ser			
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Lys	Ile	Met	Ser	Gln	Ser	Gln	Val	Ser	Lys	Gly	Val	Asp	Phe	Glu	Ser			
			675					680					685					
Ser	Glu	Asp	Asp	Asp	Asp	Asp	Pro	Phe	Met	Asn	Thr	Ser	Ser	Leu	Arg			
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 <213> Homo sapiens

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 Phe Met Glu Lys Asp Ala Ala Arg Gly Asn Asp Thr Phe Val Thr Leu
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 Asp Glu Ile Leu Arg Leu Ala Gln Glu Asn Glu Val Asp Phe Ile Leu
 35 40 45
 Leu Gly Gly Asp Leu Phe His Glu Asn Lys Pro Ser Arg Lys Thr Leu
 50 55 60
 His Thr Cys Leu Glu Leu Leu Arg Lys Tyr Cys Met Gly Asp Arg Pro
 65 70 75 80
 Val Gln Phe Glu Ile Leu Ser Asp Gln Ser Val Asn Phe Gly Phe Ser
 85 90 95
 Lys Phe Pro Trp Val Asn Tyr Gln Asp Gly Asn Leu Asn Ile Ser Ile
 100 105 110
 Pro Val Phe Ser Ile His Gly Asn His Asp Asp Pro Thr Gly Ala Asp
 115 120 125
 Ala Leu Cys Ala Leu Asp Ile Leu Ser Cys Ala Gly Phe Val Asn His
 130 135 140
 Phe Gly Arg Ser Met Ser Val Glu Lys Ile Asp Ile Ser Pro Val Leu
 145 150 155 160
 Leu Gln Lys Gly Ser Thr Lys Ile Ala Leu Tyr Gly Leu Gly Ser Ile
 165 170 175
 Pro Asp Glu Arg Leu Tyr Arg Met Phe Val Asn Lys Lys Val Thr Met
 180 185 190
 Leu Arg Pro Lys Glu Asp Glu Asn Ser Trp Phe Asn Leu Phe Val Ile
 195 200 205
 His Gln Asn Arg Ser Lys His Gly Ser Thr Asn Phe Ile Pro Glu Gln
 210 215 220
 Phe Leu Asp Asp Phe Ile Asp Leu Val Ile Trp Gly His Glu His Glu
 225 230 235 240
 Cys Lys Ile Ala Pro Thr Lys Asn Glu Gln Gln Leu Phe Tyr Ile Ser
 245 250 255
 Gln Pro Gly Ser Ser Val Val Thr Ser Leu Ser Pro Gly Glu Ala Val
 260 265 270
 Lys Lys His Val Gly Leu Leu Arg Ile Lys Gly Arg Lys Met Asn Met
 275 280 285
 His Lys Ile Pro Leu His Thr Val Arg Gln Phe
 290 295

<210> 4
 <211> 300
 <212> PRT
 <213> Saccharomyces cerevisiae

<220>
 <223> yeast MRE11 amino acids 5-304

<400> 4
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His	Glu	Val	Met	Met	Leu	Ala	Lys	Asn	Asn	Asn	Val	Asp	Met	Val	Val
		35					40					45			
Gln	Ser	Gly	Asp	Leu	Phe	His	Val	Asn	Lys	Pro	Ser	Lys	Lys	Ser	Leu
	50					55					60				
Tyr	Gln	Val	Leu	Lys	Thr	Leu	Arg	Leu	Cys	Cys	Met	Gly	Asp	Lys	Pro
65					70					75					80
Cys	Glu	Leu	Glu	Leu	Leu	Ser	Asp	Pro	Ser	Gln	Val	Phe	His	Tyr	Asp
				85					90					95	
Glu	Phe	Thr	Asn	Val	Asn	Tyr	Glu	Asp	Pro	Asn	Phe	Asn	Ile	Ser	Ile
			100					105					110		
Pro	Val	Phe	Gly	Ile	Ser	Gly	Asn	His	Asp	Asp	Ala	Ser	Gly	Asp	Ser
		115				120						125			
Leu	Leu	Cys	Pro	Met	Asp	Ile	Leu	His	Ala	Thr	Gly	Leu	Ile	Asn	His
	130					135					140				
Phe	Gly	Lys	Val	Ile	Glu	Ser	Asp	Lys	Ile	Lys	Val	Val	Pro	Leu	Leu
145					150					155					160
Phe	Gln	Lys	Gly	Ser	Thr	Lys	Leu	Ala	Leu	Tyr	Gly	Leu	Ala	Ala	Val
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Arg	Asp	Glu	Arg	Leu	Phe	Arg	Thr	Phe	Lys	Asp	Gly	Gly	Val	Thr	Phe
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		195					200					205			
His	Gln	Asn	His	Thr	Gly	His	Thr	Asn	Thr	Ala	Phe	Leu	Pro	Glu	Gln
	210					215					220				
Phe	Leu	Pro	Asp	Phe	Leu	Asp	Met	Val	Ile	Trp	Gly	His	Glu	His	Glu
225				230						235					240
Cys	Ile	Pro	Asn	Leu	Val	His	Asn	Pro	Ile	Lys	Asn	Phe	Asp	Val	Leu
				245					250					255	
Gln	Pro	Gly	Ser	Ser	Val	Ala	Thr	Ser	Leu	Cys	Glu	Ala	Glu	Ala	Gln
			260					265					270		
Pro	Lys	Tyr	Val	Phe	Ile	Leu	Asp	Ile	Lys	Tyr	Gly	Glu	Ala	Pro	Lys
		275				280						285			
Met	Thr	Pro	Ile	Pro	Leu	Glu	Thr	Ile	Arg	Thr	Phe				
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<212> PRT

<213> Artificial Sequence

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<210> 6

<211> 9

<212> PRT

<213> Artificial Sequence

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<223> Xaa = Thr or Ser

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<210> 7
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:consensus MRE11
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<210> 8
<211> 5
<212> PRT
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<212> PRT
<213> Artificial Sequence

<220>
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<210> 10
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<212> PRT
<213> Artificial Sequence

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<210> 11
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<220>
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<222> (5)
<223> Xaa = Tyr or Phe

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<210> 15
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<220>
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<210> 16
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<223> Xaa = Ile or Leu

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1 5 10

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<211> 6
<212> PRT
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<400> 18
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1 5

<210> 19
<211> 41
<212> DNA
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<223> Description of Artificial Sequence:oligonucleotide
duplex substrate for MRE11 plate-based assay

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<220>
<221> modified_base
<222> (27)
<223> n = 5-bromo-2'-deoxyuridine

<220>
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<223> n = 5-bromo-2'-deoxyuridine

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<210> 20
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:oligonucleotide
duplex substrate for MRE11 plate-based assay

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flexible linker

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or absent

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Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
35 40 45
Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
50 55 60
Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
65 70 75 80
Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
85 90 95

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			115					120					125			
Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
			130					135					140			
Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
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Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
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Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
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Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
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Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly	Gly
								200								